# (FILE 'HOME' ENTERED AT 17:31:37 ON 30 MAR 2007)

L1 L2	FILE	REGISTRY' ENTERED AT 17:31:43 ON 30 MAR 2007 STRUCTURE UPLOADED 7 S L1 FAM FULL
	FILE	CAPLUS' ENTERED AT 17:32:41 ON 30 MAR 2007
L3		203 S L2
L4		3 S L3 AND ((COMPLEX(W) REGIONAL(W) PAIN(W) SYNDROME)OR(REFLEX(W) SYM
L5		11 S L3 AND PAIN
L6		3 S L5 NOT PY>2004
L7		38 S L3 AND (TNF-ALPHA)
L8	•	11 S L7 AND (INHIBITOR OR ANTAGONIST)

=> file registry
COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FILE 'REGISTRY' ENTERED AT 17:31:43 ON 30 MAR 2007 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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STRUCTURE FILE UPDATES: 29 MAR 2007 HIGHEST RN 928707-03-3 DICTIONARY FILE UPDATES: 29 MAR 2007 HIGHEST RN 928707-03-3

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>

Uploading C:\Program Files\Stnexp\Queries\10693794elected.str

chain nodes :

8 9 18 19 20 21 22 23 24 25 26 27 28 29 30

ring nodes :

1 2 3 4 5 6 7 10 11 12 13 14 15 16 17

chain bonds :

1-9 .2-7 2-30 3-26 3-27 4-28 4-29 5-8 6-19 10-21 10-22 13-20 14-18 15-23 16-24 17-25

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-10 7-13 10-11 11-12 11-14 12-13 12-17 14-15 15-16 16-17

exact/norm bonds :

1-2 1-6 1-9 2-3 2-7 3-4 4-5 5-6 5-8 7-10 7-13 10-11 12-13 13-20 14-18

exact bonds :

2-30 3-26 3-27 4-28 4-29 6-19 10-21 10-22 15-23 16-24 17-25 normalized bonds :

11-12 11-14 12-17 14-15 15-16 16-17

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:CLASS 9:CLASS 10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS

20:CLASS 21:CLASS

22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS

30:CLASS

#### L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

Structure attributes must be viewed using STN Express query preparation.

=> s l1 fam full

FULL SEARCH INITIATED 17:32:04 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 262 TO ITERATE

100.0% PROCESSED 262 ITERATIONS

SEARCH TIME: 00.00.01

L2 7 SEA FAM FUL L1

=> d 12 scan

L2 7 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2,6-Piperidinedione, 3-(4-amino-1,3-dihydro-1-oxo-2H-isoindol-2-yl)-, (-)(9CI)

7 ANSWERS

MF C13 H13 N3 O3

Rotation (-).

## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):4

L2 7 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2,6-Piperidinedione, 3-(4-amino-1,3-dihydro-1-oxo-2H-isoindol-2-yl)-,

(3R) - (9CI)

MF C13 H13 N3 O3

Absolute stereochemistry.

## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L2 7 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

MF C13 H13 N3 O3 . 1/2 H2 O

## ●1/2 H<sub>2</sub>O

- L2 7 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
- IN 2,6-Piperidinedione, 3-(4-amino-1,3-dihydro-1-oxo-2H-isoindol-2-yl)-
- MF C13 H13 N3 O3
- CI COM

## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L2 7 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2,6-Piperidinedione, 3-(4-amino-1,3-dihydro-1-oxo-2H-isoindol-2-yl)-, (+)(9CI)

MF C13. H13 N3 O3

Rotation (+).

## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 68.15 68.36

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 17:32:41 ON 30 MAR 2007 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 30 Mar 2007 VOL 146 ISS 15 FILE LAST UPDATED: 29 Mar 2007 (20070329/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html => s 12 L3 203 L2 => s 13 and ((complex(w)regional(w)pain(w)syndrome)or(Reflex(w)sympathetic(w)dystrophy)) 1329086 COMPLEX 67862 REGIONAL 49424 PAIN 123930 SYNDROME 110 COMPLEX (W) REGIONAL (W) PAIN (W) SYNDROME 25143 REFLEX 39834 SYMPATHETIC 13005 DYSTROPHY 175 REFLEX (W) SYMPATHETIC (W) DYSTROPHY L43 L3 AND ((COMPLEX(W) REGIONAL(W) PAIN(W) SYNDROME) OR (REFLEX(W) SYMPAT HETIC(W)DYSTROPHY)) => d l4 1-3 ti abs bib ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN L4Methods and compositions using immunomodulators for the treatment, ΤI prevention or management of dysfunctional sleep and dysfunctional sleep associated with disease AB Methods are disclosed for treating, preventing and/or managing dysfunctional sleep, including but not limited to, dysfunctional sleep associated with chronic neurol. or inflammatory condition such as pain and neurodegenerative disorders, which comprise the administration of one or more immunomodulatory compds. or a pharmaceutically acceptable salt, solvate, stereoisomer, clathrate or prodrug thereof, alone or in combination with known therapeutics. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed. Immunomodulatory compds. include e.g. 4-amino-2-[2,6-dioxo(3-piperidyl)]isoindoline-1,3-dione. AN DN 143:339698 TI Methods and compositions using immunomodulators for the treatment, prevention or management of dysfunctional sleep and dysfunctional sleep associated with disease IN Zeldis, Jerome B.; Manning, Donald C.; Faleck, Herbert PA SO U.S. Pat. Appl. Publ., 21 pp. CODEN: USXXCO DT Patent LA English FAN.CNT 1 PATENT NO. KIND APPLICATION NO. DATE DATE ---------PΤ US 2005222209 **A1** 20051006 US 2005-93848 20050330 AU 2005231415 A1 20051020 AU 2005-231415 20050331 CA 2561910 Α1 20051020 CA 2005-2561910 20050331 WO 2005097125 A2 WO 2005-US10937 20051020 20050331 WO 2005097125 **A3** 20070125 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

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PRAI US 2004-559261P
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     WO 2005-US10937
                             W
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     ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
T.4
ΤI
     Methods of using and compositions comprising immunomodulatory compounds
      for treatment, modification, and management of pain
AB
     Methods for treating, preventing, modifying and managing various types of
     pain are disclosed. Specific methods comprise the administration of an
      immunomodulatory compound, or a pharmaceutically acceptable salt, solvate,
     hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in
     combination with a second active agent and/or surgery, psychol. or phys.
      therapy. Pharmaceutical compns., single unit dosage forms, and kits
      suitable for use in methods of the invention are also disclosed.
     2005:426405 CAPLUS <<LOGINID::20070330>>
ΑN
DN
     142:457122
     Methods of using and compositions comprising immunomodulatory compounds
TI
      for treatment, modification, and management of pain
IN
      Zeldis, Jerome B.; Faleck, Herbert; Manning, Donald C.
PA
     Celgene Corporation, USA
SO
     PCT Int. Appl., 62 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 5
     PATENT NO.
                           KIND
                                   DATE
                                                APPLICATION NO.
                                                                           DATE
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PRAI US 2003-693794
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     US 2002-421003P
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                                   20021024
     WO 2004-US12721
                            W
                                   20040423
os
     MARPAT 142:457122
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- L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Methods of using and compositions comprising immunomodulatory compounds for treatment, modification and management of pain

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AB Methods of treating, preventing, modifying and managing various types of pain are disclosed. Specific methods comprise the administration of an immunomodulatory compound of formula (I), or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or surgery, psychol. or phys. therapy. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

AN 2004:368888 CAPLUS <<LOGINID::20070330>>

DN 140:368712

TI Methods of using and compositions comprising immunomodulatory compounds for treatment, modification and management of pain

IN Zeldis, Jerome B.; Faleck, Herbert; Manning, Donald C.

PA Celgene Corporation, USA

SO PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 5

	PATENT	NO.			KIND DATE				APPL	ICAT		DATE						
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	EP 155	6044			A2		2005	0727	EP 2003-777871						20031024			
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	BR 200										003-							
	CN 173				A						003-							
	JP 200								•	JP 2	004-	5471	26		20	0031	024	
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os	WO 200				W		2003	1024										
US	MARPAT	140:	200/.	14														

=> s l3 and pain

49424 PAIN

L5 11 L3 AND PAIN

=> s 15 not py>2004 2909281 PY>2004

#### => d 16 1-3 ti

- L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Treatment of low back pain and whiplash-associated disorder with, for example, a monoclonal antibody, an antisense oligonucleotide, or an MMP inhibitor
- L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Use of a TNF inhibitor for the treatment of low back pain
- L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Formulations of adenosine A1 agonists

#### => d 16 1-11 ti

- L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Treatment of low back pain and whiplash-associated disorder with, for example, a monoclonal antibody, an antisense oligonucleotide, or an MMP inhibitor
- L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Use of a TNF inhibitor for the treatment of low back pain
- L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Formulations of adenosine A1 agonists

#### => d 15 1-11 ti

- L5 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of dioxopiperidinyl-isoindolone and -isoindolediones derivatives as antitumor agents
- L5 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Multicyclic sulfonamide compounds as inhibitors of histone deacetylase for the treatment of disease and their preparation
- L5 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Method of using, and compositions comprising, immunomodulatory compounds for the treatment and management of myeloproliferative diseases
- L5 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Methods and compositions using immunomodulators for the treatment, prevention or management of dysfunctional sleep and dysfunctional sleep associated with disease
- L5 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Methods of using and compositions comprising immunomodulatory compounds for treatment, modification, and management of pain
- L5 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Methods of using and compositions comprising immunomodulatory compounds for the treatment and management of myeloproliferative diseases
- L5 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Methods of using and compositions comprising immunomodulatory compounds for treatment, modification and management of pain
- L5 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Method using dialkyl ethers and other compounds for treating arthritis, cartilage damage, and other interleukin 6-mediated conditions

L5 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

TI Treatment of low back pain and whiplash-associated disorder with, for example, a monoclonal antibody, an antisense oligonucleotide, or an MMP inhibitor

L5 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

TI Use of a TNF inhibitor for the treatment of low back pain

L5 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

TI Formulations of adenosine A1 agonists

# => d 15 2 3 5 6 7 9 10 11 ti abs bib

L5 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

TI Multicyclic sulfonamide compounds as inhibitors of histone deacetylase for the treatment of disease and their preparation

GI

Disclosed herein are sulfonamide compds. of formula I as described herein. AΒ Compds. of formula I wherein G1 is bond, alkenyl, alkoxy, alkoxyalkyl, alkyl, alkylamino, alkylcarbonyl, etc.; G2 is (un) substituted (mono/poly) heteroaryl; G3 is SO2NH and derivs., NHSO2 and derivs., C1-3 alkyl-SO2NH and derivs., and NHSO2-C1-3 alkyl and derivs.; G4 is bicyclic (hetero)aryl, and (hetero)cycloalkyl-fused monocyclic (hetero)aryl; W is OH and derivs., (un) substituted oxyalkyl, SH and derivs., etc.; R1 is H, PO3H2 and derivs., CN, (un) substituted acyl, (hetero) aryl, alkyl, aroyl, etc.; R2 and R3 are independently H, Me, and Et; and their therapeutically acceptable salts, esters, and prodrugs thereof, are claimed. Methods and compns. are disclosed for treating disease states including, but not limited to cancers, autoimmune diseases, tissue damage, central nervous system disorders, neurodegenerative disorders, fibrosis, bone disorders, polyglutamine-repeat disorders, anemias, thalassemias, inflammatory conditions, cardiovascular conditions, and disorders in which angiogenesis play a role in pathogenesis, using the compds. of the invention. In addition, methods of modulating the activity of histone deacetylase (HDAC) are also disclosed. Example compound II was prepared by chlorination of 6-chloronicotinic acid; the resulting 6-chloronicotinoyl chloride underwent alkylation of di-Me malonate to give di-Me 2-(6chloronicotinoy1) malonate, which underwent decarboxylation to give

2-chloro-5-acetylpyridine, which underwent amination to give 2-amino-5-acetylpyridine, which underwent sulfamidation with 2,3-dihydrobenzo[1,4]dioxin-6-sulfonyl chloride to give 2,3-dihydrobenzo[1,4]dioxin-6-sulfonic acid (5-acetylpyridin-2-yl)amide, which underwent bromination to give 2,3-dihydrobenzo[1,4]dioxin-6-sulfonic acid (5-(bromoacetyl)pyridin-2-yl)amide, which underwent substitution with potassium thioacetate to give compound II. All the invention compds. were evaluated for their HDAC inhibitory activity. From the assay, it was determined that compound II exhibited in vitro and cellular IC50 values of  $\leq 1 \mu M$ . 2007:119480 CAPLUS <<LOGINID::20070330>> 146:206220 Multicyclic sulfonamide compounds as inhibitors of histone deacetylase for the treatment of disease and their preparation Malecha, James W.; Noble, Stewart A.; Wiley, Brandon M.; Hoffman, Timothy Z.; Bonnefous, Celine; Sertic, Michael; Wash, Paul L.; Smith, Nicholas D.; Hassig, Christian A.; Scranton, Shawn A.; Payne, Joseph E.; Hager, Jeffery Kalypsys, Inc., USA U.S. Pat. Appl. Publ., 44pp. CODEN: USXXCO Patent English FAN.CNT 1 PATENT NO. KIND APPLICATION NO. DATE DATE -------------------US 2007027184 **A**1 20070201 US 2006-496784 20060727 WO 2007016354 A1 20070208 WO 2006-US29438 20060727 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM PRAI US 2005-704091P P 20050729 US 2006-780129P P 20060307 MARPAT 146:206220 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN Method of using, and compositions comprising, immunomodulatory compounds for the treatment and management of myeloproliferative diseases

- L5
- ΤI
- AB Methods of treating, preventing, and/or managing a myeloproliferative disease are disclosed. Specific methods encompass the administration of an immunomodulatory compound, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent, and/or the transplantation of blood or cells. Particular second active agents are capable of suppressing the overprodn. of hematopoietic stem cells or ameliorating one or more of the symptoms of a myeloproliferative disease. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.
- AN
- DN 144:17165

AN

DN

ΤI

TN

PA

SO

DT

LA

PΙ

os

- ΤI Method of using, and compositions comprising, immunomodulatory compounds for the treatment and management of myeloproliferative diseases
- IN Zeldis, Jerome B.
- PA Celgene Corporation, USA
- PCT Int. Appl., 59 pp. SO CODEN: PIXXD2

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DT
     Patent.
     English
LA
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     PATENT NO.
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                         A1
                               20051201
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    EP 1746995
                         Α1
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                                           EP 2004-751399
                                                                  20040505
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PRAI WO 2004-US14003
                               20040505
                         Α
    MARPAT 144:17165
RE.CNT 6
             THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
L5
    ANSWER 5 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
TΤ
    Methods of using and compositions comprising immunomodulatory compounds
    for treatment, modification, and management of pain
AΒ
    Methods for treating, preventing, modifying and managing various types of
    pain are disclosed. Specific methods comprise the administration
    of an immunomodulatory compound, or a pharmaceutically acceptable salt,
    solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in
    combination with a second active agent and/or surgery, psychol. or phys.
    therapy. Pharmaceutical compns., single unit dosage forms, and kits
     suitable for use in methods of the invention are also disclosed.
ΑN
    DN
    142:457122
TI
    Methods of using and compositions comprising immunomodulatory compounds
    for treatment, modification, and management of pain
IN
    Zeldis, Jerome B.; Faleck, Herbert; Manning, Donald C.
PA
    Celgene Corporation, USA
SO
    PCT Int. Appl., 62 pp.
    CODEN: PIXXD2
DT
    Patent
LA
    English
FAN.CNT 5
    PATENT NO.
                        KIND
                               DATE
                                           APPLICATION NO.
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ΡI
    WO 2005044178
                         A2
                               20050519
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            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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20050915

US 2003-693794

20031023

A1

TD, TG

US 2005203142

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      EP 1680111
                            A2
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                                   20070117
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                            Α
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                            W
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os
      MARPAT 142:457122
      ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
L5
      Methods of using and compositions comprising immunomodulatory compounds
TI
      for the treatment and management of myeloproliferative diseases
AΒ
      Methods of treating, preventing and/or managing a myeloproliferative
      disease are disclosed. Specific methods encompass the administration of
      an immunomodulatory compound, or a pharmaceutically acceptable salt,
      solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in
      combination with a second active agent, and/or the transplantation of
      blood or cells. Particular second active agents are capable of
      suppressing the overprodn. of hematopoietic stem cells or ameliorating one
      or more of the symptoms of a myeloproliferative disease. Pharmaceutical
      compns., single unit dosage forms, and kits suitable for use in methods of
      the invention are also disclosed. The immunomodulatory compound is especially
      4-(amino)-2-[2,6-dioxo(3-piperidyl)]isoindoline-1,3-dione or
      3-(4-amino-1-oxo-1,3-dihydroisoindol-2-yl)piperidine-2,6-dione.
AN
      2004:372856 CAPLUS <<LOGINID::20070330>>
DN
      140:368680
TI
     Methods of using and compositions comprising immunomodulatory compounds
      for the treatment and management of myeloproliferative diseases
IN
      Zeldis, Jerome B.
PA
     U.S. Pat. Appl. Publ., 20 pp.
SO
     CODEN: USXXCO
DТ
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
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                                               APPLICATION NO.
                                                                         DATE
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                                                                         20030411
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                                   20040527
                                                CA 2003-2504663
                                                                         20030413
     WO 2004043464
                            A1
                                   20040527
                                                WO 2003-US11328
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         UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
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     AU 2003241289
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                            A1
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                                                EP 2003-731018
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     BR 2003016082
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                                   20050927
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                                                JP 2004-551395
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                                   20060727
                                                US 2006-371777
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PRAI US 2002-424730P
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     US 2003-411656
                          A3
                                   20030411
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WO 2003-US11328

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20030413

ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN  $L_5$ 

Methods of using and compositions comprising immunomodulatory compounds TI for treatment, modification and management of pain

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 & R^2 & N \\
 & N & N
\end{array}$$

$$\begin{array}{c|c}
 & H & \\
 & N & N \\
\end{array}$$

Methods of treating, preventing, modifying and managing various types of AB pain are disclosed. Specific methods comprise the administration of an immunomodulatory compound of formula (I), or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or surgery, psychol. or phys. therapy. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

2004:368888 CAPLUS <<LOGINID::20070330>> AN

DN 140:368712

TIMethods of using and compositions comprising immunomodulatory compounds for treatment, modification and management of pain

IN Zeldis, Jerome B.; Faleck, Herbert; Manning, Donald C.

PA Celgene Corporation, USA

SO PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DTPatent

LA English

FAN.	CNT 5						
	PATENT NO.	KIND DATE	APPLICATION NO.	DATE			
ΡI	WO 2004037199		WO 2003-US33757	20031024			
	WO 2004037199	A3 20041223					
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	GH, GM, HR,	HU, ID, IL, IN,	IS, JP, KE, KG, KP, KR,	KZ, LC, LK,			
			MG, MK, MN, MW, MX, MZ,				
			SC, SD, SE, SG, SK, SL,				
			UZ, VC, VN, YU, ZA, ZM,				
	RW: GH, GM, KE,	LS, MW, MZ, SD,	SL, SZ, TZ, UG, ZM, ZW,	AM, AZ, BY,			
			BE, BG, CH, CY, CZ, DE,				
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			CA 2003-2503536				
			AU 2003-286663				
			EP 2003-777871				
			GB, GR, IT, LI, LU, NL,				
			CY, AL, TR, BG, CZ, EE,				
			BR 2003-15609				
	CN 1732000		CN 2003-80107531				
			JP 2004-547126				
PRAI	US 2002-421003P			<b>-</b>			
	WO 2003-US33757	W 20031024					
os	MARPAT 140:368712						

- TI Treatment of low back pain and whiplash-associated disorder with, for example, a monoclonal antibody, an antisense oligonucleotide, or an MMP inhibitor
- AB The use of a substance that inhibits disk-related nerve-irritating substances for the production of a pharmaceutical composition for treatment of low

back pain and/or whiplash-associated disorder (WAD) is disclosed. The substance that inhibits disk-related nerve-irritating substances is, e.g., a monoclonal antibody, a soluble cytokine receptor or a receptor antagonist, an antisense oligonucleotide, an MMP inhibitor, a quinolone, a thalidomide derivative, an inhibitor of IL-1, IL-6, IL-8, or IFN- $\gamma$ , and a nitric oxide or eicosanoid blocking substance. Also a method for treatment of low back pain and/or whiplash-associated disorder (WAD) is disclosed. For example, a male patient diagnosed with sciatica due to disk herniation and whiplash-associated disorder (pain in the region of the neck that radiated out into both arms after a vehicle accident) was treated with an i.v. injection of 2.5 mL of Orthogen (an IL-1 receptor antagonist) dissolved in 2.5 mL saline. The day after the injection, the patient reported that the sciatic pain was markedly reduced. His problems in the neck region were also greatly improved and minor stiffness in the neck and the radiating pain in the arms had more or less disappeared. At the follow-up examination 1 wk later, he reported that he only suffered minor pain in the legs and also in the neck. Four weeks after the injection, the patient considered himself free of symptoms, and this was the case also at the final follow-up examination at 8 wk.

- AN 2002:793397 CAPLUS <<LOGINID::20070330>>
- DN 137:289029
- TI Treatment of low back pain and whiplash-associated disorder with, for example, a monoclonal antibody, an antisense oligonucleotide, or an MMP inhibitor
- IN Olmarker, Kjell; Rydevik, Bjoern
- PA A+ Science Invest AB, Swed.
- SO PCT Int. Appl., 35 pp.
- CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 1

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. P	PATENT NO.							DATE		APPLICATION NO.						DATE				
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PI W	VO 2	2002080893			A1	A1 200210			7 WO 2002-SE673							20020405				
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			FI,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,		
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	•		CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,		
			BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG		
PRAI S	SE 2	2001-	-125	3		Α		2001	0406											
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS										S RE	CORD									

- L5 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Use of a TNF inhibitor for the treatment of low back pain

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The use of a tumor necrosis factor (TNF) inhibitor for the production of a pharmaceutical composition for treatment of low back pain and in particular of low back pain due to local irritation of annulus-related nerve fibers by disk derived substances is described. Also a method for treatment of low back pain is disclosed. For example, a patient was given infliximab, a selective monoclonal antibody that inhibits only TNF, at 5 mg/kg for treatment of low back pain

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to feel symptoms of relief regarding his pain. The improvement
     was found to be dramatic at the follow-up examns. and persisted during 4
     wk.
     AN
DN
     137:304790
     Use of a TNF inhibitor for the treatment of low back pain
TΙ
IN
     Olmarker, Kjell; Rydevik, Bjoern
PA
     A+ Science Invest AB, Swed.
SO
     PCT Int. Appl., 29 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                        KIND
                               DATE
                                          APPLICATION NO.
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PΙ
     WO 2002080891
                               20021017
                                         WO 2002-SE671
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                        Α
PRAI SE 2001-1256
                               20010406
RE.CNT 8
             THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
L5
     ANSWER 11 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
TI
     Formulations of adenosine A1 agonists
     A method of treating conditions associated with pain and
AB
     alleviating the symptoms associated with it comprises administering to a
     mammal an adenosine Al agonist or a salt or solvate and an NSAID, e.g., a
     COX-2 inhibitor. The present invention also provides pharmaceutical
     formulations and patient packs comprising the combinations. Thus,
     (2S, 3S, 4R, 5R) -2-(5-tert-butyl-[1,3,4]oxadiazol-2-yl)-5-[6-(4-chloro-2-
     fluorophenylamino)purin-9-yl]tetrahydrofuran-3,4-diol (I) was prepared in a
     series of steps by the reaction of (3aS,4S,6R,6aR)-6-(6-chloropurin-9-yl)-
     2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxole-4-carboxylic acid with
     2,2-dimethylpropionic acid hydrazide followed by the cyclization of the
    resulting compound, and subsequent treatment with 4-chloro-2-fluoroaniline
     and deprotection. I and 2-(4-ethoxy-phenyl)-3-(4-
    methanesulfonylphenyl)pyrazolo[1,5-b]pyridazine(COX-2 inhibitor), were
    administered at 1% to rats. The compds. showed inhibition of
    carrageenan-induced edema and allodynia.
AN
    DN
    135:81971
TI
    Formulations of adenosine Al agonists
IN
    Bountra, Charanjit; Clayton, Nicholas Maughan; Naylor, Alan
PA
    Glaxo Group Limited, UK
    PCT Int. Appl., 33 pp.
so
    CODEN: PIXXD2
DT
    Patent
    English
LA
FAN.CNT 1
                       KIND
                              DATE
                                          APPLICATION NO.
                                                                DATE
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ΡI
    WO 2001045683
                        A2
                              20010628
                                          WO 2000-GB4883
                                                                20001219
    WO 2001045683
                       A3
                              20020314
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            CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
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Approx. 1.5 h after completing the administration the patient started

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HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
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             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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                                            EP 2000-985627
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     EP 1239879
                                20020918
                          A2
     EP 1239879
                                20040225
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                          Т
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     AT 260119
                                20040315
                                                                  20001219
                                            US 2002-168195
     US 2003004128
                          A1
                                20030102
                                                                   20020618
PRAI GB 1999-30075
                          Α
                                19991220
     WO 2000-GB4883
                          W
                                20001219
=> s 13 and (TNF-alpha)
         67328 TNF
       1676057 ALPHA
         50526 TNF-ALPHA
                 (TNF(W)ALPHA)
L7
            38 L3 AND (TNF-ALPHA)
=> s 17 and (inhibitor or antagonist)
        535258 INHIBITOR
        167898 ANTAGONIST
            11 L7 AND (INHIBITOR OR ANTAGONIST)
1.8
=> d 18 1-11 ti
     ANSWER 1 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
L8
     Cytokine targets in the treatment of myelodysplastic syndromes
ΤI
L8
     ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
TI
     Combination therapy comprising a cyclooxygenase 2 (COX-2)
     inhibitor and an antineoplastic agent for treatment or prevention
     of neoplasia
     ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
L8
ΤI
     Immunological abnormalities in hematological diseases
     ANSWER 4 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
L8
     Combinations for the treatment of diseases involving cell proliferation,
TΙ
     migration or apoptosis of myeloma cells, or angiogenesis
     ANSWER 5 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
rs
TI
     Methods of using and compositions comprising immunomodulatory compounds
     for the treatment and management of myelodysplastic syndromes
     ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
L8
ΤI
     Combination therapy including a JNK kinase inhibitor for
     treating, preventing or managing proliferative disorders and cancers
     ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
L8
ΤI
     CC-5013: Treatment of multiple myeloma treatment of melanoma treatment of
     myelodysplastic syndrome angiogenesis inhibitor TNF-.
     alpha. production inhibitor
     ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
L8
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Preparation of 2-(2,6-dioxo-3-piperidyl)isoindoline-1,3-diones, related

inhibitors for treatment of cancer, inflammatory disorders, heart disease,

compounds, and compositions thereof as  $TNF-\alpha$ 

ΤI

### and related disorders

- L8 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Immunomodulatory drug CC-5013 overcomes drug resistance and is well tolerated in patients with relapsed multiple myeloma
- L8 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of 2-(2,6-dioxo-3-piperidyl)isoindoline-1,3-diones, related compounds, and compositions thereof as  $TNF-\alpha$  inhibitors for treatment of cancer, inflammatory disorders, heart disease, and related disorders
- L8 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Amino-substituted thalidomide analogs: potent inhibitors of TNF  $-\alpha$  production

#### => d 18 2 5 7 8 9 10 11 ti abs bib

- L8 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Combination therapy comprising a cyclooxygenase 2 (COX-2) inhibitor and an antineoplastic agent for treatment or prevention of neoplasia
- AB . A method for treating or preventing neoplasia or a neoplasia-related disorder in a subject is provided, the method comprising administering to the subject an effective amount of a combination comprising a COX-2 inhibitor and an antineoplastic agent.
- AN 2005:470251 CAPLUS <<LOGINID::20070330>>
- DN 143:19957
- TI Combination therapy comprising a cyclooxygenase 2 (COX-2) inhibitor and an antineoplastic agent for treatment or prevention of neoplasia
- IN Masferrer, Jaime L.
- PA Pharmacia Corporation, USA
- SO PCT Int. Appl., 317 pp. CODEN: PIXXD2
- DT Patent
- LA English
- FAN CNT 1

FAN.	CNT 1						
	PATENT NO.	KIND DATE	APPLICATION NO.	DATE			
ΡI	WO 2005048942	A2 2005060:	2 WO 2004-US38019	20041115			
	WO 2005048942	A3 2006033	)				
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			, DM, DZ, EC, EE, EG, ES,				
	GE, GH, GM	, HR, HU, ID, IL	, IN, IS, JP, KE, KG, KP,	KR, KZ, LC,			
	LK, LR, LS	, LT, LU, LV, MA	, MD, MG, MK, MN, MW, MX,	MZ, NA, NI,			
	NO, NZ, OM	, PG, PH, PL, PT	, RO, RU, SC, SD, SE, SG,	SK, SL, SY,			
	TJ, TM, TN	, TR, TT, TZ, UA	, UG, US, UZ, VC, VN, YU,	ZA, ZM, ZW			
			NA, SD, SL, SZ, TZ, UG,				
			TM, AT, BE, BG, CH, CY,				
			IE, IS, IT, LU, MC, NL,				
	SE, SI, SK	, TR, BF, BJ, CF	CG, CI, CM, GA, GN, GQ,	GW, ML, MR,			
	NE, SN, TD	, TG					
	US 2005227929	A1 20051013	US 2004-989192	20041115			
PRAI	US 2003-519701P	P 20031113	<b>}</b>				

- L8 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Methods of using and compositions comprising immunomodulatory compounds for the treatment and management of myelodysplastic syndromes
- AB Methods of treating, preventing and/or managing myelodysplastic syndromes are disclosed. Specific methods encompass the administration of immunomodulatory compound, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in

combination with a second active ingredient, and/or the transplantation of blood or cells. Specific second active ingredients are capable of affecting or improving blood cell production Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed. Patients with myelodysplastic syndromes were treated orally with 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione.

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AN 2004:354803 CAPLUS <<LOGINID::20070330>>
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DN 140:350572

TI Methods of using and compositions comprising immunomodulatory compounds for the treatment and management of myelodysplastic syndromes

IN Zeldis, Jerome B.

PA Celgene Corporation, USA

SO PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.							KIND DATE			APPLICATION NO.							DATE			
PI	WO 2004035064				A1 20040429				WO 2	003-										
		W:							ΑZ,											
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			LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,		
			PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	ΤJ,	TM,	TN,	TR,	TT,	TZ,		
									ZA,									-		
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			FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	ΝL,	PT,	RO,	SE,	SI,	SK,	TR,		
			BF,	ВJ,	CF,	CG,			GΑ,											
	US 2004220144							1104		US 2	003-4	4116	49		20	030	411			
	US 7189740																			
										· CA 2003-2477301										
							A1 20040504				AU 2003-228508									
	EP	14874				A1			1222								00304			
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			IE,	SI,	LT,	LV,			MK,								SK			
		2003							0816								00304	113		
		17139							1228								00304	113		
		2006							0302		JP 2						00304	113		
DD 3 -		20070				A		2007		1	JP 2	006-2	2781	02		20	0061	11		
PRAI								2002:										,		
		2004						2003												
00	WO 2003-US11323 W MARPAT 140:350572							2003	0413											
os	MAH	(PAT	140:3	35057	72															

- RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L8 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI CC-5013: Treatment of multiple myeloma treatment of melanoma treatment of myelodysplastic syndrome angiogenesis inhibitor TNF-. alpha. production inhibitor
- AB A review. Due to its immunomodulatory activity, thalidomide has shown efficacy as a treatment in several inflammatory diseases involving increased tumor necrosis factor (TNF) levels. However, thalidomide has also been shown to be effective in noninflammatory diseases such as cancer. Thalidomide displayed potent antiangiogenic activity and has shown efficacy in trials involving patients with advanced and refractory myeloma, resulting in complete and near-complete responses and increases in survival. Unfortunately, thalidomide continues to be associated with significant adverse effects, which has prompted a search for novel potent analogs with reduced toxicity. The thalidomide analogs discovered have been classified into 2 groups: selective cytokine-inhibitory drugs

(SeICIDS) and immunomodulatory drugs (IMiDs). CC-5013 has emerged as an effective IMiD, displaying TNF- $\alpha$  -inhibitory, antiangiogenic, cytokine-related and immunomodulatory effects more potent than thalidomide but without the adverse neurol. effects. CC-5013 has been shown to be safe and effective in phase I and II trials in patients with relapsed and refractory multiple myeloma and myelodysplastic syndrome and is now in phase III development for these indications.

AN 2003:704643 CAPLUS <<LOGINID::20070330>>

DN 139:285454

TI CC-5013: Treatment of multiple myeloma treatment of melanoma treatment of myelodysplastic syndrome angiogenesis inhibitor TNF-. alpha. production inhibitor

AU Sorbera, L. A.; Castaner, J.; Bayes, M.

CS Prous Science, Barcelona, 08080, Spain

SO Drugs of the Future (2003), 28(5), 425-431 CODEN: DRFUD4; ISSN: 0377-8282

PB Prous Science

DT Journal; General Review

LA English

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

TI Preparation of 2-(2,6-dioxo-3-piperidyl)isoindoline-1,3-diones, related compounds, and compositions thereof as TNF- $\alpha$  inhibitors for treatment of cancer, inflammatory disorders, heart disease, and related disorders

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II

AB The invention relates to isoindole-imide compds. and pharmaceutically acceptable salts, hydrates, solvates, clathrates, enantiomers, diastereomers, racemates, or mixts. of stereoisomers thereof, pharmaceutical compns. comprising these isoindole-imide compds., and methods for reducing the level of cytokines and their precursors in mammals. In particular, the invention pertains to isoindole-imide compds. that are potent inhibitors of the production of TNF-.alpha. in mammals. The isoindole-imides described herein are useful for treating or preventing diseases or disorders in mammals, for example,

cancers, such as solid tumors and blood-born tumors; heart disease, such as congestive heart failure; osteoporosis; and genetic, inflammatory; allergic; and autoimmune diseases. Title isoindole-imides I [wherein one of X and Y is CO and the other is CH2 or CO; R1 = H, (cyclo)alkyl, alkenyl, alkynyl, benzyl, aryl, alkylheterocycloalkyl, alkylheteroaryl, COR3, CSR3, CO2R4, alkyl-(NR6)2, alkyl-OR5, alkyl-CO2R5, CONHR3, CSNHR3, CON(R3)2, CSN(R3)2, or alkyl-OCOR5; R2 = H, benzyl, alkyl, alkenyl, or alkynyl; R3 = independently (cyclo)alkyl, alkenyl, alkynyl, benzyl, aryl, alkylheterocycloalkyl, alkylheteroaryl, alkyl-N(R6)2, alkyl-OR5, alkyl-CO2R5, alkyl-OCOR5, or CO2R5; R4 = alkyl, alkenyl, alkynyl, alkyl-OR5, benzyl, aryl, alkylheterocycloalkyl, or alkylheteroaryl; R5 = alkyl, alkenyl, alkynyl, benzyl, aryl, or heteroaryl; R6 = independently H, alkyl, alkenyl, alkynyl, benzyl, (hetero)aryl, or alkyl-CO2R5; or R6 groups may join to form a heterocycloalkyl group; n = 0-1; with the proviso that when n = 0,  $R1 \neq H$ ; or pharmaceutically acceptable salts, hydrates, solvates, clathrates, enantiomers, diastereomers, racemates, or mixts. of stereoisomers thereof] were prepared for reducing the level of cytokines and their precursors in mammals. In particular, the invention pertains to isoindole-imide compds. that are potent inhibitors of the production of TNF- $\alpha$  (no data). For example, Me 2-(methoxycarbonyl)-3-nitrobenzoate was hydrogenated with 10% Pd/C (87%). The amine was converted to the nitrile by diazonium salt formation effected by treatment with NaNO3 followed by cyanide formation using classic Sandmeyer procedure (65%). The nitrile was reduced with 10% Pd/C in MeOH and aqueous HCl under hydrogen to afford Me 3-aminomethyl-2-(methoxycarbonyl)benzoate•HCl (90%), which was treated with TEA and then reacted with di-t-Bu dicarbonate to give the carbamate (93%). Cyclization with 3-aminoglutarimide HCl using diisopropylethylamine in DMF produced II (82%). The 2-(2,6-dioxo-3-piperidyl)isoindoline-1,3diones and pharmaceutical compns. comprising them are useful for treating or preventing diseases or disorders in mammals, e.g. cancers, such as solid tumors and blood-born tumors; heart disease, such as congestive

AN 2003:396458 CAPLUS <<LOGINID::20070330>>

autoimmune diseases (no data).

- DN 138:385311
- TI Preparation of 2-(2,6-dioxo-3-piperidyl)isoindoline-1,3-diones, related compounds, and compositions thereof as TNF- $\alpha$  inhibitors for treatment of cancer, inflammatory disorders, heart disease, and related disorders

heart failure; osteoporosis; and genetic, inflammatory, allergic, and

- IN Robarge, Michael J.; Chen, Roger Shen-Chu; Muller, George W.; Man, Hon-Wah PA USA
- SO U.S. Pat. Appl. Publ., 100 pp., CCont.-in-part of U.S. Ser. No. 972,487. CODEN: USXXCO
- DT Patent
- LA English
- FAN.CNT 2

	PA.	<b>TENT</b>	NO.			KIN	D	DATE		AP	PLIC	DATE							
PI		2003096841				A1 B2	-	2003	0522 0815	US	200	01-3	32286	5 5		20	0011	221	
	US	2003	0455	52		A1		2003	0306	US 2001-972487							20011005		
	ΑT	3525	48			${f T}$		2007	0215	AT	200	1-9	9713	33		20	0011	221	
	EP	1767	533			<b>A1</b>		2007	0328	EP	EP 2006-17608						20011221		
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			NL,	PT,	SE,	TR,	ΑL,	LT,	LV,	MK, R	o, s	ΞI							
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	US	2006	0255	97		A1		2006	0202	US	200	5-2	3044	18		20	050	921	
	JP	2006	08949	95		Α		2006	0406	JP	JP 2005-321049						0051	104	
	. AU	2006	2007	17		A1		2006	0316	AU	200	6-2	007	17		20	060	221	
PRAI	US	2000	-2583	372P		P		2000	1227										
	US	2001	-9724	487		A2		2001	1005										
	AU	2002	-2482	252		A3		2001	1221										
	ΕP	2001	-997	133		<b>A3</b>		2001	1221			•							

JP 2002-559408 A3 20011221 US 2001-32286 A3 20011221

OS MARPAT 138:385311

RE.CNT 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L8 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Immunomodulatory drug CC-5013 overcomes drug resistance and is well tolerated in patients with relapsed multiple myeloma
- AB Thalidomide (Thal) can overcome drug resistance in multiple myeloma (MM) but is associated with somnolence, constipation, and neuropathy. in vitro studies, we have shown that the potent immunomodulatory derivative of thalidomide (IMiD) CC-5013 induces apoptosis or growth arrest even in resistant MM cell lines and patient cells, decreases binding of MM cells to bone marrow stromal cells (BMSCs), inhibits the production in the BM milieu of cytokines (interleukin-6 [IL-6], vascular endothelial growth factor [VEGF], tumor necrosis factor- $\alpha$  [ TNF- $\alpha$  ]) mediating growth and survival of MM cells, blocks angiogenesis, and stimulates host anti-MM natural killer (NK) cell immunity. Moreover, CC-5013 also inhibits tumor growth, decreases angiogenesis, and prolongs host survival in a human plasmacytoma mouse model. In the present study, we carried out a phase 1 CC-5013 dose-escalation (5 mg/d, 10 mg/d, 25 mg/d, and 50 mg/d) study in 27 patients (median age 57 yr; range, 40-71 yr) with relapsed and refractory relapsed MM. They received a median of 3 prior regimens (range, 2-6 regimens), including autologous stem cell transplantation and Thal in 15 and 16 patients, resp. In 24 evaluable patients, no dose-limiting toxicity (DLT) was observed in patients treated at any dose level within the first 28 days; however, grade 3 myelosuppression developed after day 28 in all 13 patients treated with 50 mg/d CC-5013. In 12 patients, dose reduction to 25 mg/d was well tolerated and therefore considered the maximal tolerated dose (MTD). Importantly, no significant somnolence, constipation, or neuropathy has been seen in any cohort. Best responses of at least 25% reduction in paraprotein occurred in 17 (71%) of 24 patients (90% confidence interval [CI], 52%-85%), including 11 (46%) patients who had received prior Thal. Stable disease (less than 25% reduction in paraprotein) was observed in an addnl. 2 (8%) patients. Therefore, 17 (71%) of 24 patients (90% CI, 52%-85%) demonstrated benefit from treatment. Our study therefore provides the basis for the evaluation of CC-5013, either alone or in combination, to treat patients with MM at earlier stages of disease.
- AN 2002:840111 CAPLUS <<LOGINID::20070330>>
- DN 138:83060
- TI Immunomodulatory drug CC-5013 overcomes drug resistance and is well tolerated in patients with relapsed multiple myeloma
- AU Richardson, Paul G.; Schlossman, Robert L.; Weller, Edie; Hideshima, Teru; Mitsiades, Constantine; Davies, Faith; LeBlanc, Richard; Catley, Laurence P.; Doss, Deborah; Kelly, Kathleen; McKenney, Mary; Mechlowicz, Julie; Freeman, Andrea; Deocampo, Reggie; Rich, Rebecca; Ryoo, Joan J.; Chauhan, Dharminder; Balinski, Kathe; Zeldis, Jerome; Anderson, Kenneth C.
- CS Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
- SO Blood (2002), 100(9), 3063-3067 CODEN: BLOOAW; ISSN: 0006-4971
- PB American Society of Hematology
- DT Journal
- LA English
- RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L8 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of 2-(2,6-dioxo-3-piperidyl)isoindoline-1,3-diones, related compounds, and compositions thereof as TNF- $\alpha$  inhibitors for treatment of cancer, inflammatory disorders, heart disease, and related disorders

Ι

ΙI

Title isoindole-imides I [wherein one of X and Y is CO and the other is AB CH2 or CO; R1 = H, (cyclo)alkyl, alkenyl, alkynyl, benzyl, aryl, alkylheterocycloalkyl, alkylheteroaryl, COR3, CSR3, CO2R4, alkyl-(NR6)2, alkyl-OR5, alkyl-CO2R5, CONHR3, CSNHR3, CON(R3)2, CSN(R3)2, or alkyl-OCOR5; R2 = H, benzyl, alkyl, alkenyl, or alkynyl; R3 = independently (cyclo) alkyl, alkenyl, alkynyl, benzyl, aryl, alkylheterocycloalkyl, alkylheteroaryl, alkyl-N(R6)2, alkyl-OR5, alkyl-CO2R5, alkyl-OCOR5, or CO2R5; R4 = alkyl, alkenyl, alkynyl, alkyl-OR5, benzyl, aryl, alkylheterocycloalkyl, or alkylheteroaryl; R5 = alkyl, alkenyl, alkynyl, benzyl, aryl, or heteroaryl; R6 = independently H, alkyl, alkenyl, alkynyl, benzyl, (hetero)aryl, or alkyl-CO2R5; or R6 groups may join to form a heterocycloalkyl group; n = 0-1; with the proviso that when n = 0,  $R1 \neq H$ ; or pharmaceutically acceptable salts, hydrates, solvates, clathrates, enantiomers, diastereomers, racemates, or mixts. of stereoisomers thereof] were prepared for reducing the level of cytokines and their precursors in mammals. In particular, the invention pertains to isoindole-imide compds. that are potent inhibitors of the production of  $TNF-\alpha$  (no data). For example, Me 2-(methoxycarbonyl)-3-nitrobenzoate was hydrogenated with 10% Pd/C (87%). The amine was converted to the nitrile by diazonium salt formation effected by treatment with NaNO3 followed by cyanide formation using classic Sandmeyer procedure (65%). The nitrile was reduced with 10% Pd/C in MeOH and aqueous HCl under hydrogen to afford Me 3-aminomethyl-2-(methoxycarbonyl)benzoate HCl (90%), which was treated with TEA and then reacted with di-t-Bu dicarbonate to give the carbamate (93%). Cyclization with 3-aminoglutarimide HCl using diisopropylethylamine in DMF produced II (82%). The 2-(2,6-dioxo-3-piperidyl)isoindoline-1,3diones and pharmaceutical compns. comprising them are useful for treating or preventing diseases or disorders in mammals, e.g. cancers, such as solid tumors and blood-born tumors; heart disease, such as congestive heart failure; osteoporosis; and genetic, inflammatory, allergic, and autoimmune diseases (no data).

AN 2002:575064 CAPLUS <<LOGINID::20070330>>

DN 137:125091

TI Preparation of 2-(2,6-dioxo-3-piperidyl)isoindoline-1,3-diones, related compounds, and compositions thereof as  $TNF-\alpha$ 

inhibitors for treatment of cancer, inflammatory disorders, heart disease, and related disorders Robarge, Michael J.; Chen, Roger Shen-Chu; Muller, George W.; Man, Hon-Wah IN PA Celgene Corporation, USA SO PCT Int. Appl., 224 pp. CODEN: PIXXD2 DT Patent English LA FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE ----------------------------WO 2002059106 **A1** 20020801 WO 2001-US50401 20011221 PΙ W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2003045552 A1 20030306 US 2001-972487 20011005 CA 2433021 A1 20020801 CA 2001-2433021 20011221 EP 2001-997133 EP 1363900 20031126 20011221 **A1** EP 1363900 20070124 B1 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR HU 2003-2578 HU 200302578 **A2** 20031128 20011221 JP 2004525889 Т 20040826 JP 2002-559408 20011221 NZ 526893 20051028 NZ 2001-526893 20011221 Α AT 352548 т 20070215 AT 2001-997133 20011221 EP 1767533 A1 20070328 EP 2006-17608 20011221 AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI ZA 2003005759 20050117 ZA 2003-5759 20030101 Α JP 2006089495 20060406 JP 2005-321049 Α 20051104 AU 2006200717 Α1 20060316 AU 2006-200717 20060221 PRAI US 2000-258372P 20001227 P US 2001-972487 A 20011005 AU 2002-248252 A3 20011221 EP 2001-997133 А3 20011221 JP 2002-559408 Α3 20011221 WO 2001-US50401 W 20011221 MARPAT 137:125091 OS THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 7 ALL CITATIONS AVAILABLE IN THE RE FORMAT ANSWER 11 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN L8 TI Amino-substituted thalidomide analogs: potent inhibitors of TNF  $-\alpha$  production Thalidomide is a known inhibitor of TNF-.alpha ABrelease in LPS stimulated human PBMC. Herein we describe the  $TNF-\alpha$  inhibitory activity of amino substituted analogs of thalidomide and its isoindolin-1-one analog, EM-12. 4-amino substituted analogs were found to be potent inhibitors of TNF- $\alpha$  release in LPS stimulated human PBMC. AN DN 131:129881 Amino-substituted thalidomide analogs: potent inhibitors of TNF TI  $-\alpha$  production Muller, George W.; Chen, Roger; Huang, Shaei-Yun; Corral, Laura G.; Wong, ΑU Lu Min; Patterson, Rebecca T.; Chen, Yuxi; Kaplan, Gilla; Stirling, David

Celgene Corporation, Warren, NJ, 07059, USA

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